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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/583,848	05/31/2000	Beatrice Gaugler	LUD 5353.7 DIV (10016357)	4358

24972 7590 04/14/2004

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EXAMINER	
DAVIS, MINH TAM B	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 04/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/583,848	GAUGLER ET AL.	
	Examiner	Art Unit	
	MINH-TAM DAVIS	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *75-80* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *75-80* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. 03/29/04
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Applicant cancels claims 1-74, and adds new claims 75-80, which are related to claims 55-56, 63-64, 66-74.

Accordingly, claims 75-80 are being examined.

The following are the remaining rejections.

REJECTION UNDER 35 USC 112, SECOND PARAGRAPH, NEW REJECTION

Claim 78 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 78 recites the limitation "vectors" in claim 76. There is insufficient antecedent basis for this limitation in the claim.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, NEW MATTER, NEW REJECTION

Claims 75-80 are rejected under 35 USC 112, first paragraph, as the specification does not contain a written description of the claimed invention.

Claims 75-80 are drawn to an isolated cDNA molecule which encodes a polypeptide that is processed, intracellularly to a peptide that is encoded by nucleotides

70-96 of SEQ ID NO:18, wherein said isolated cDNA molecule comprises the nucleotide sequence of SEQ ID NO:18, a vector and a host cell comprising said cDNA molecule.

The limitation of "a cDNA molecule which encodes a polypeptide that is processed, intracellularly to a peptide that is encoded by nucleotides 70-96 of SEQ ID NO:18" claimed in Claims 75-80 has no clear support in the specification and the claims as originally filed.

It is noted that although US 5,405,940 was incorporated by reference by the instant application, as argued by Applicant on page 5 of the response of 01/09/04, and although in the interview of 27 August 2003, Applicant pointed out that nucleotides 70-96 of the 225 nucleotide sequence of SEQ ID NO:18 of the claimed invention encode a 9 amino acid peptide which is the same as SEQ ID NO:9 of MAGE-6 recited in US 5,405,940 (US 5,405,940, first page and claims 1, 8), a review of the instant specification and US 5,405,940 indicates lack of support in the instant specification for the limitation of "a cDNA molecule which encodes a polypeptide that is processed, intracellularly to a peptide that is encoded by nucleotides 70-96 of SEQ ID NO:18". There is support in the instant application for SEQ ID NO:18 (page 9, line 16, and Example 32, pages 35-36, and processing of the sequences coding for tumor rejection antigen precursors into tumor rejection antigens (p.44, lines 12-14). There is support in Application 938,334, now patented US 5,405,940 for the nonapeptide of SEQ ID No:9, which is encoded by nucleotides 70-96 of SEQ ID NO:18 of the instantly claimed invention. However, it appears that the instant claims encompass new larger genus of sequences,encoding a polypeptide that need to only to include the peptide encoded by

nucleotides 70-96 of SEQ ID NO:18, such that it is processed to the nonapeptide, and are not limited to just SEQ ID NO:18, or a polynucleotide consisting of nucleotides 70-96 of SEQ ID NO:18 and encoding the nonapeptide of SEQ ID NO:9, for which support is found.

The subject matter claimed in claims 75-80 broadens the scope of the invention as originally disclosed in the specification.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, WRITTEN DESCRIPTION, NEW REJECTION

The instant specification does not contain a written description of the invention in such full, clear, concise, and exact terms or in sufficient detail that one skilled in the art can reasonably conclude that applicant had possession of the claimed invention at the time of filing.

Claims 75-80 are rejected under 35 USC 112, first paragraph, as lacking an adequate written description in the specification.

Claims 75-80 drawn to an isolated cDNA molecule which encodes a polypeptide that is processed, intracellularly to a peptide that is encoded by nucleotides 70-96 of SEQ ID NO:18, wherein said isolated cDNA molecule "comprises" the nucleotide sequence of SEQ ID NO:18, a vector and a host cell comprising said cDNA molecule.

It is noted that SEQ ID NO:18 is only a small fragment of full length MAGE-6. The specification discloses that SEQ ID NO:18 is a cDNA of 225 nucleotides prepared from mRNAs of a melanoma cell line (specification, p.9, line 16, and Example 32 on page 35-

35). The art discloses that a polynucleotide sequence domain of MAGE-6 seems to comprise about 4-5kb, and that MAGEs-(1-12) polynucleotides that have been sequenced span in the range of 3kb to 4.5kb (De Plaen et all, 1994, of record). Thus it is reasonable to interpret that the polynucleotide of SEQ ID NO:18 in the claimed invention is only a small cDNA fragment of full length MAGE-6 polynucleotide.

Due to the language "comprises", claims 75-80 encompass any nucleic acid containing SEQ ID NO:18, which Applicant had not reduced to practice at the time of filing, wherein said nucleic acid could have any sequences attached to the defined fragment, SEQ ID NO:18, provided it is in frame with SEQ ID NO:18. There is no limitation as to the nature of the molecules attached to SEQ ID NO:18. The present claim encompasses full-length genes and cDNAs that are not further described.There is substantial variability among the species of DNAs encompassed within the scope of the claims because SEQ ID NO:18 is only a fragment of any full-length gene or cDNA species. "A cDNA comprising SEQ ID NO:18" encompasses a variety of subgenera with widely varying attributes .For example,a cDNA 's principle attribute would include its coding region.A partial cDNA that did not include a disclosure of any open reading frame (ORF)of which it would be a part,would not be representative of the genus of cDNAs because no information regarding the coding capacity of any cDNA molecule would be disclosed.

Although the specification discloses a single cDNA fragment consisting of SEQ ID NO:18, this does not provide a description of a cDNA molecule comprising the

nucleotide sequence of SEQ ID NO:18, and encoding a polypeptide that is processed intracellularly to a peptide that is encoded by nucleotides 70-96 of SEQ ID NO:18.

The instant disclosure of a single species of nucleic acid does not adequately describe the scope of the claimed genus, which encompasses a substantial variety of subgenera including full-length genes. A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). The specification fails to describe a cDNA molecule comprising the nucleotide sequence of SEQ ID NO:18, and encoding polypeptide that is processed intracellularly to a peptide that is encoded by nucleotides 70-96 of SEQ ID NO:18, by the test set out in Lilly. The specification describes only a single cDNA fragment consisting of SEQ ID NO:18. Therefore, it necessarily fails to describe a "representative number" of species of cDNA molecules comprising the nucleotide sequence of SEQ ID NO:18, and encoding a polypeptide that is processed intracellularly to a peptide that is encoded by nucleotides 70-96 of SEQ ID NO:18.

One of skill in the art would conclude that Applicant was not in possession of the genus of polynucleotides comprising a polynucleotide fragment, SEQ ID NO:18, and encoding a polypeptide that is processed intracellularly to a peptide that is encoded by nucleotides 70-96 of SEQ ID NO:18.

Thus, the specification does not provide an adequate written description of a cDNA molecule "comprising" the nucleotide sequence of SEQ ID NO:18, and encoding a polypeptide that is processed intracellularly to a peptide that is encoded by nucleotides 70-96 of SEQ ID NO:18, that is required to practice the claimed invention.

REJECTION UNDER 35 USC 112 FIRST PARAGRAPH, SCOPE

New claims 75-80 are rejected under 112, first paragraph, because the specification, while being enabling for an isolated cDNA molecule which encodes a polypeptide that is processed, intracellularly to a peptide that is encoded by nucleotides 70-96 of SEQ ID NO:18, wherein said isolated cDNA molecule "consists of " the nucleotide sequence of SEQ ID NO:18, does not reasonably provide enablement for an isolated cDNA molecule which encodes a polypeptide that is processed, intracellularly to a peptide that is encoded by nucleotides 70-96 of SEQ ID NO:18, wherein said isolated cDNA molecule "comprises" the nucleotide sequence of SEQ ID NO:18.

New claims 75-80 drawn to an isolated cDNA molecule which encodes a polypeptide that is processed, intracellularly to a peptide that is encoded by nucleotides 70-96 of SEQ ID NO:18, wherein said isolated cDNA molecule "comprises" the nucleotide sequence of SEQ ID NO:18, a vector and a host cell comprising said cDNA molecule.

Applicant argues on page 5 that the claim 75 recites functional language, i.e. the cDNA encodes a polypeptide that is processed, intracellularly to a peptide that is encoded by nucleotides 70-96 of SEQ ID NO:18. Applicant asserts that the peptide is

described in U.S. Patent No. 5,405,940, referred to in prior correspondence, and that the '940 patent was incorporated by reference, in view of page 6, lines 22-24.

Applicant further argues that turning to the specific objections raised by the Examiner, the Examiner has determined that she can ignore a prior USPTO determination that this peptide functions as a tumor rejection antigen. Applicant asserts that patents are presumed enabled, and the '940 patent expressly states and claims that the peptide referred to *supra* is a tumor rejection antigen.

This argument is found not to be persuasive. Although U.S. Patent No. 5,405,940 is referred to in the instant application, reciting the nonapeptide of SEQ ID NO:9, it is noted that whether the '940 patent recites that said peptide functions as a tumor rejection is not germane, because each case is decided on its own facts. It is well settled that whether similar claims have been allowed to others is immaterial. See In re Giolito, 530 F.2d 397, 188 USPQ 645 (CCPA 1976) and Ex parte Balzarini 21 USPQ2d 1892, 1897 (BPAI 1991).

Applicant asserts on page 5 that the peptide the nucleotides 70-96 of SEQ ID NO: 18 encodes is EVDPIGHVY as shown in the attached paper by Benlalam, et al., 2003, especially page 6286, second column.

Applicant asserts on page 6 that when one considers the relevant art, such as US 6,552,180, US5,686,068, US6,565,857, US 6,488,932, the paper by Benlalam or Kobayashi, showing that MAGE-2, MAGE-3, MAGE-4 and MAGE-6 stimulate CTLs, one expects MAGE molecules, including MAGE-A6, to be processed to peptides presented by HLA molecules to form T cell provoking complexes.

Applicant asserts on page 6 that the Examiner has referred to the "comprising" langùage of claim 74, but since new claim 75 requires a specific peptide to be encoded, the argument is moot. Applicant asserts that indeed, it is noted that the Examiner clearly notes at page 4, that SEQ ID NO: 18 is part of a larger molecule. Hence, the Examiner's position is contrary to the extent it is understood.

The recitation of Benlalam, et al., 2003 and Kobayashi, et al (2003), and US patents US5,405,940, US6,552,180, US5,686,068, US6,565,857 and 6,488,932 is acknowleged and entered.

Applicant's arguments are not persuasive, because SEQ ID NO:18 is only a small fragment of full length MAGE-6, *supra*, and the claims are not limited to just SEQ ID NO:18 . Due to the language "comprises", claims 75-80 encompass any nucleic acid containing SEQ ID NO:18 of any length, wherein said nucleic acid could have any sequences attached to the defined fragment, SEQ ID NO:18, provided it is in frame with SEQ ID NO:18. There is no limitation as to the nature of the molecules attached to SEQ ID NO:18.

Applicant has not taught how to make the claimed numerous sequences comprising SEQ ID NO:18 that would be reasonably expected to be processed as claimed. For example, Applicant has not taught what the structure is for the sequences attached to the defined fragment, SEQ ID NO:18, or what the coding regions are for these sequences, or what proteins are encoded by these sequences. Further, one could not predict whether that the claimed sequences would encode a protein having the property of being processed intracellularly to said nonapeptide, in view of teaching in

the art that protein chemistry is unpredictable, and that even a single amino acid substitution or what appear to be an inconsequential chemical modification will often dramatically affect the biological activity and characteristics of a protein, as taught by Bowie et al, Burgess et al, Lazar et al, Tao et al and Gillies e tal, all of record, and that such unpredictability would apply as well to the encoding polynucleotide. Thus the requirement of "encoding a polypeptide that is processed intracellularly to a peptide encoded by nucleotides 70-96 of SEQ ID NO:18" is not sufficient to impart eitheir characteristic physical, structural or functional features to the claimed numerous cDNA molecules "comprising" SEQ ID NO:18, or any common property with other members of the MAGE family.

Further, since the claimed sequences would have any sequences, which are in frame with SEQ ID NO:18 and attached to SEQ ID NO:18, one cannot predict how the additional sequences would affect intracellular processing of the polypeptides encoded by the claimed nucleic acid molecules. It is well known in the art that the ability of intracellular processing of a polypeptide by proteasomes to peptides to be presented to the MHC molecules depends on the structure and stability of said polypeptide (Kirkin et al, 1998, of record, p.673, second column, second paragraph). Kirkin et al teach that "in order to be presented to the MHC molecules, intracellular antigens should undergo several steps of antigen processing, and that important steps in this process are ubiquitination of the denatured protein followed by proteolytic cleavage of the polypeptide chain in proteasomes". Kirkin further teach that "high stability of the structure reduces the denaturation of the protein and thus ubiquitination as a

degradation signal". In addition, Kirkin et al teach that "in order to gain acess to the inner proteolytic component of the barrel-shaped proteasome, the polypeptide has to be unfolded, and that the efficiency of this energy-requiring unfolding should depend on the protein structure, alpha-helical conformation is known to provide the optimal geometry for maximal amount of strength of the hydrogen bonds formed". Thus based on the teaching in the art and in the specification, one cannot predict how the sequences added to SEQ ID NO:18 would affect intracellular processing of the polypeptides encoded by the claimed nucleic acid molecules. Applicant however has not taught how to make the claimed cDNA molecules such that it encodes a polypeptide that could be processed intracellularly to a peptide that is encoded by nucleotides 70-96 of SEQ ID NO:18.

Applicant asserts on page 6 that Applicant does not follow the argument at page 9 et seq, and that the activity attributed to MAGE molecules is their processing to immunoreactive peptides, and that this is all that is required. Applicant asserts that further, it is shown that the MAGE family behaves this way generally.

The Office action at page 9 in previous Office action was to show that Applicant has not taught how to make the claimed cDNA molecules, in view that 1) SEQ ID NO:18 is only a small fragment of full length MAGE-6, and 2) the claimed sequences encompass sequences unrelated to SEQ ID NO:18.

In view of the above, and previous Office action, Applicant is not enabled for an isolated cDNA molecule which encodes a polypeptide that is processed, intracellularly to a peptide that is encoded by nucleotides 70-96 of SEQ ID NO:18, wherein said

isolated cDNA molecule "comprises" the nucleotide sequence of SEQ ID NO:18, a vector and a host cell comprising said cDNA molecule.

It is noted that Applicant is invited to amend the claims to recite the closed language "consisting of" rather than "comprises" in claim 75 to obviate the above 112, first paragraph rejections.

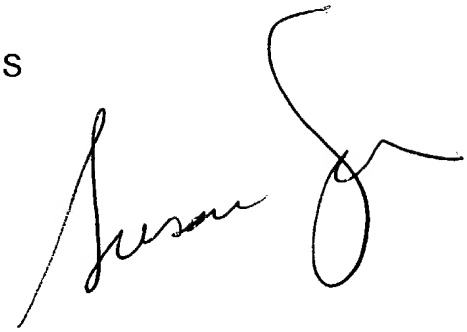
Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 571-272-0830. The examiner can normally be reached on 9:30AM-4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, YVONNE EYLER can be reached on 571-272-0871. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MINH TAM DAVIS

March 31, 2004



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